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BOLD responses in reward regions to hypothetical and imaginary monetary rewards

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Abstract

Monetary rewards are uniquely human. Because money is easy to quantify and present visually, it is the reward of choice for most fMRI studies, even though it cannot be handed over to participants inside the scanner. A typical fMRI study requires hundreds of trials and thus small amounts of monetary rewards per trial (e.g. 5p) if all trials are to be treated equally. However, small payoffs can have detrimental effects on performance due to their limited buying power. Hypothetical monetary rewards can overcome the limitations of smaller monetary rewards but it is less well known whether predictors of hypothetical rewards activate reward regions. In two experiments, visual stimuli were associated with hypothetical monetary rewards. In experiment 1, we used stimuli predicting either visually presented or imagined hypothetical monetary rewards, together with non-rewarding control pictures. Activations to reward predictive stimuli occurred in reward regions, namely the medial orbitofrontal cortex and midbrain. In experiment 2, we parametrically varied the amount of visually presented hypothetical monetary reward keeping constant the amount of actually received reward. Graded activation in midbrain was observed to stimuli predicting increasing hypothetical rewards. The results demonstrate the efficacy of using hypothetical monetary rewards in fMRI studies.

INTRODUCTION

Money is a strong motivator. Subjects work harder, more persistently, and more effectively, if they earn more money for better performance (Camerer & Hogarth, 1999). Typical fMRI studies involve hundreds of trials with each trial lasting around 10 seconds. If one wants to treat each trial equally and incentive-compatible, then monetary rewards paid to the participants per trial need to be small to avoid excessive expenditure for the experimenter. Gneezy and Rustichini (2000) found that while larger amounts of money yielded higher performance (in terms of parents complying with day care rules), smaller amounts yielded poorer performance than no compensation at all. Hence, monetary incentives at low value can have a detrimental effect on performance. Hypothetical payoffs provide one possibility to overcome the limitation of small gambles in experimental situations (Kahneman & Tversky, 1979).

Hypothetical rewards have been investigated in behavioural studies using paradigms such as the Iowa gambling task (Bowman & Turnbull, 2003; Fernie & Turney, 2006) and temporal discounting tasks (Johnson & Bickel, 2002; Lagorio & Madden, 2005). These previous studies suggest that hypothetical rewards can motivate behaviour to a similar degree as actual rewards (but see Holt & Laury, 2002). In a neuroimaging study, Wittman et al. (2007) investigated temporal discounting using hypothetical rewards in the range of few hundred dollars with delays ranging from 5 days to 10 years. However, hypothetical rewards have also been used for much shorter delays (e.g. in Gregorios-Pippas et al., 2009, where participants received a percentage of displayed reward every trial). Neural findings from these earlier studies using hypothetical rewards were in line with other imaging studies of temporal discounting using potentially real rewards (e.g. McClure et al., 2004, where one of the participant's choices was selected randomly). In agreement with this notion, Bickel et al. (2009) found no difference in behavioural and neural activation when comparing real and hypothetical monetary gains and fictive monetary losses in a temporal discounting task. Thus, at least in situations involving future

outcomes, hypothetical monetary rewards seem to be able to influence behaviour and neural activity similar to real payoffs.

Monetary rewards are secondary reinforcers that possibly acquired their value by association with more primary rewards. It is therefore conceivable that monetary rewards act through imagination of rewarding objects that can be acquired through them. Indeed in a recent reward imagination study by Bray et al. (2010), participants who imagined monetary or other types of secondary rewards activated primary reward regions. However, monetary rewards have become so ubiquitous in our daily life that they can be considered as rewards in their own right. Functional neuroimaging studies using monetary rewards have found the same brain regions as those involved in processing primary rewards also without asking participants to imagine (e.g. Valentin & O'Doherty, 2009; Tobler et al., 2007; Kim et al., 2011). Given that money is easier to present than primary rewards, it is no surprise that monetary rewards have become the choice of most neuroimaging studies of reward processing. We set out to investigate motivational aspects and corresponding neural activity using various different ways of presenting hypothetical monetary rewards.

Human neuroimaging studies using blood-oxygen-level-dependent (BOLD) functional magnetic resonance imaging (fMRI) have identified a set of reward regions in the midbrain, striatum and orbitofrontal cortex, consistent with findings from non-human primates (for review see Haber & Knutson, 2010). Moreover, conditioned stimuli predicting real monetary rewards activate reward regions in humans (e.g. Tobler et al., 2007). Here, we set out to investigate whether also predictors of hypothetical monetary rewards would activate reward regions of the brain. In order to investigate motivational aspects of monetary rewards, we presented participants with hypothetical rewards that displayed a larger value, but told them that they would be able to take home only a specific percentage of the displayed money. Some previous studies (e.g. Dreher et al., 2006; Kuhnen & Knutson, 2005; Gregorios-Pippas et al., 2009) have used a similar strategy but not explicitly studied the effects of hypothetical rewards. Accordingly, we

performed two experiments using different scenarios – when the hypothetical rewards are visually presented or imagined (experiment 1) and when the real pay-off is explicitly displayed (experiment 2) or invisible (experiment 1). Further we hypothesized that increasing the hypothetical monetary reward would result in increased activation in reward regions although the real pay-off is kept constant (experiment 2).

Materials and Methods

Subjects

A total of 17 right handed participants (mean age 25.5 years, range 21.6 - 30.5 years) were recruited from among undergraduate and graduate student populations in the Cambridge area of the UK. Ten participants took part in both the experiments (the first experiment was always performed at the end of the session). The data from two participants could not be recovered due to technical reasons. The data from three participants, from each of the two experiments, were excluded from all analyses due to large head movements detected in the realignment process. The final data analysis was performed on 12 participants each in the first (5 female) and second (6 female) experiments. Participants were pre-assessed through self-report to exclude prior histories of neurological or psychiatric illness (including depression and schizophrenia), and drug usage. Participants were asked to refrain from excessive alcohol usage on the night before scanning. All participants gave informed written consent and were paid for participation. The research protocol was approved by the Cambridgeshire Local Research Ethics Committee, U.K.

Stimuli, training and pleasantness ratings

Scanning only took place after participants had learned the meaning of abstract visual stimuli in a training session (see below). Experiment 1 used a 2x2 factorial design in which four abstract stimuli were paired with visually presented or imagined hypothetical monetary reward or a control picture. During the imagination trials, a blank screen was displayed following the offset of the abstract stimulus. Experiment 2 used a 2x3 factorial

design in which six abstract stimuli were paired with pictorial or alphanumerical display of parametrically increasing hypothetical monetary rewards with three different magnitudes. The hypothetical monetary rewards were always accompanied by a fixed real-payoff (5 pence) that was invisible (experiment 1) or explicitly displayed (experiment 2). The stimulus-reward associations were randomized across subjects for both experiments. The presentation of the stimuli and recording of responses was controlled by Cogent 2000 software on Matlab.

For both experiments 1 and 2, we trained subjects up to a week before the scanning session to learn the correct stimulus-reward contingencies (Figure 1a). Stimulus pleasantness ratings for the abstract stimuli were collected from the subjects before and after training and scanning sessions (Figure 1a). The abstract stimuli were rated on a scale of 1 (dislike very much) to 5 (like very much). The value of 3 was marked as indifferent on the pleasantness rating scale. After baseline pleasantness ratings were collected, participants received a customized instruction sheet, showing the exact stimulus-reward contingencies. After reading the instructions, participants returned the instruction sheet to the experimenter. The training session proceeded with identical trial structure (see descriptions below) as the scanning session except that the number of repetitions for each trial type in the training session was half (experiment 1: 15, experiment 2: 20) of those in the scanning session.

Experiment 1

In experiment 1 (Figure 1b), four visual (fractal) stimuli predicted either visual presentation or imagination of a money bill (reward) or a scrambled picture (no reward). The rewarding picture was a hypothetical monetary reward (£20 money bill) together with an invisible real payoff (5 pence) that was added to the cumulative sum to take home at the end of the experiment. The non-rewarding picture was a scrambled picture of a £20 money bill that did not contribute towards cumulative earnings. The scrambled picture was smoothed to avoid any overt association with the £20 money bill or reconstruction of

the money bill from its parts. The visual presentation and imagination trials differed in that the money bill (hypothetical reward) and the scrambled picture were displayed on the screen or not, respectively.

Each trial started with a central fixation '+' symbol at the centre of the screen, presented during a truncated Poisson distributed random interval (mean 4 sec; maximum duration 6 sec). Then, one of the four visual stimuli appeared for 2 sec. The offset of the visual stimulus marked the onset of a 1 sec presentation of the rewarding picture (£20 money bill) or the scrambled picture for visual presentation trials or of a blank screen for imagination trials. At the end of every trial, one of the two questions "what did you see" or "what did you imagine" appeared on the screen. Below the question, three answer choices (money bill; scrambled picture; nothing) were indicated. Participants responded by pressing one of three corresponding buttons. The spatial position of the three answer choices on the screen was randomized across trials to avoid preparation of specific movements during stimulus presentation. Including the option of having seen or imagined "nothing" allowed us to get reliable self-report from the participants. If the participant did not respond within 1.5 sec, a red square was flashed for 0.5 sec and the trial was repeated. Cumulative earnings were not displayed to prevent explicit pairing of the visual stimuli with the visual receipt of the reward in the imagination trials. Unbeknownst to the participants, a total of 30 repetitions for each trial type were required to complete the scanning session.

In this experiment, we particularly ensured that participants successfully understand the meaning of stimuli that predicted imagination of the money bill or the scrambled picture by the customized instruction sheet. No further explicit instructions were given during the experiment regarding imagination. Hence, participants never experienced a visible (hypothetical or real) reward in the imagination trials in either the training or scanning sessions. We adopted this strategy so that the training and scanning sessions were identical. Learning was ensured by including a question at the end of every trial (as indicated above).

Experiment 2

Experiment 2 investigated effects of parametrically increasing hypothetical rewards without increasing the actual pay-off (Figure 1c). Six abstract stimuli were associated with three values of alphanumeric or pictorial displayed money – 10 pence, 1 Pound and 10 Pounds, all predicting the same amount of real money (5 pence). Participants were informed before the experiment that all displayed money was hypothetical whereas actual cumulative earnings were displayed at the bottom of the screen throughout the experiment. To control for visual saliency, we presented both pictures of real money and alphanumeric representations of the three values. Monetary rewards were visually presented at a uniform size of 240x120 pixels.

Each trial started with a central fixation '+' symbol at the centre of the screen, presented during a random interval that followed a truncated Poisson distribution (mean 5 sec; maximum duration 8 sec). This interval served to separate the present from the previous trial. Then, one of the six visual stimuli (dimensions 100x100 pixels) appeared for 2 sec at a random location either on the top-half or on the bottom-half of the screen. A conditional motor task was overlaid onto the Pavlovian paradigm to keep participants attentive throughout the experiment. Participants responded by pressing either the left or right button (using a mouse in training sessions and an MRI compatible button box in scanning sessions) with their index and middle fingers, respectively, to indicate where on the screen the stimulus had appeared. The allocation of top half-to-left button vs. top half-to-right button was randomized across participants. After a correct response, the monetary reward was visually presented for 1 sec replacing the abstract stimulus on the screen. Upon error, a red square was shown at the centre of the screen and the trial was repeated. The cumulative sum of actual money received was displayed throughout at the bottom of the screen, and was updated at the time of displaying the monetary reward. A total of 40 repetitions for each trial type were required to complete two scanning runs. The counter of cumulative earnings was reset in-between two scanning runs.

To ensure learning of stimulus-reward contingencies, participants were tested on a modified version of the task immediately after the training session. The testing task consisted of displaying one abstract stimulus at a time at the centre top half of the screen and the six sets of monetary rewards in two rows at the bottom of the screen. Subjects indicated the monetary reward associated with the abstract stimulus displayed by pressing the appropriate key on a keypad.

Data Acquisition and Analysis

This section describes imaging data acquisition and analysis for both experiments. Functional imaging was performed on a MedSpec (Bruker, Ettlingen, Germany) scanner at 3 Tesla. Two whole brain acquisitions weighted by Gradient Echo and Spin Echo were obtained within a scan repetition time (TR) of 2.4 sec. 21 horizontal slices with in-plane resolution of 3.75mm x 3.75mm, were collected with a slice thickness of 5 mm and slice gap of 1 mm. We used Statistical Parametric Mapping (SPM2) software from the Wellcome Department of Cognitive Neurology, London within Matlab 6.5 (The Mathworks Inc., MA) for data analysis. The first five volumes of each series were discarded to avoid T1 saturation effects. Results from the Gradient Echo acquisition are reported as no additional activation was observed with the Spin Echo acquisition.

Data Analysis:

Images were slice-time corrected and realigned to correct for any head movements. The realigned images were normalized to a standard brain EPI template in MNI (Montreal Neurological Institute) space (Friston et al., 1995a) and resampled to a voxel size of 2x2x2 mm. An isotropic Gaussian filter with 8 mm full width at half maximum was used to spatially smooth the normalized images. Serial autocorrelations within the functional data were estimated using a first order auto-regressive model (AR-1). Statistical analysis was performed using a general linear model (Friston et al., 1995b). The data were high-pass filtered at a frequency of 1/128 Hz. Given that the stimulus-outcome associations had already been learnt during the training session by our participants, activations were assessed at the onset of the abstract visual stimuli predicting reward or no reward

(experiment 1) or hypothetical rewards of different magnitudes (experiment 2). Stick functions at the onset of the visual stimuli were convolved with a canonical hemodynamic response function (HRF) and its time and dispersion derivatives. Group analysis was performed with random effects models (Penny et al., 2003) and correction for non-sphericity of the data.

Thresholding strategy

Based on previous neurophysiological and human neuroimaging studies of reward and novelty, we defined three regions of interest (ROIs) in the midbrain (Schultz, 1998; Elliott et al., 2003; O'Doherty et. al., 2006; Bunzeck & Düzel, 2006; Tobler et al., 2007), ventral striatum (Knutson et al., 2001; O'Doherty et. al., 2006; Burke et al., 2010) and medial orbitofrontal cortex (O'Doherty et al., 2001; Bray et al., 2010; Sescousse et al., 2010) in agreement with their known role in reward processing. All ROIs were anatomically defined using the WFU Pick Atlas toolbox (Lancaster et al., 2000; Maldjian et al., 2003). The ROI for the midbrain consisted of bilateral substantial nigra extended by 2 mm to include the medially adjoining ventral tegmental area (VTA). Given the similarity of neurophysiological responses of dopamine neurons in the ventral tegmental area and the substantia nigra pars compacta (Schultz, 1998), we did not focus on either of these structures (D'Ardenne et al., 2008; Düzel et al., 2009). The ROI for ventral striatum was anatomically defined consisting of caudate and putamen confined to brain slices $z < 0$ mm and extended by 2 mm to include the medially adjoining nucleus accumbens. The ROI for medial OFC was anatomically defined. Reported activations are corrected for multiple comparisons ($p<0.05$, family-wise error) for height of activation within the volume of our ROI. For visualization of the extent of activations in our ROIs (in figures and activation table), we use an exploratory threshold of $p<0.005$ uncorrected with a minimum extent of 10 voxels.

Behavioural Results

Pleasantness ratings of abstract stimuli did not differ before training (experiment 1: $F(3,33)=0.49$, $p=0.69$; experiment 2: $F(5,66)=0.59$, $p=0.7$). Participants successfully

learned the stimulus-reward associations by the end of the training session for both experiments (Figure 2).

In experiment 1, the stimuli predicting reward were rated as more pleasant than the control stimuli predicting no reward (visual presentation: $p<0.005$, imagination: $p<0.05$). In experiment 2, stimuli associated with 10 pounds were rated as more pleasant than stimuli associated with 10 pence (alphanumeric: $p<0.05$, pictorial: $p<0.05$). Learning, as indexed by change in pleasantness ratings, was significant during the training session (experiment 1: $p<0.05$, experiment 2: $p<0.05$). No further learning took place during the scanning session (first experiment: $p=0.07$, second experiment: $p=0.12$). These results suggest that the stimulus-reward associations were successfully established during the training session, which took place up to a week before the scanning session.

In experiment 1, all participants correctly reported the contents of visual presentation and imagination (money bill or scrambled picture) at the end of every trial in more than 94% of trials (average 96.8%±1%) in the scanning session. In experiment 2, participants correctly identified stimulus-reward associations (accuracy ranging between 83.6±7% and 93.3±3.5%) during the testing session immediately after the training session. These results indicate the correct identification of stimulus-reward associations.

Brain Imaging

Activation to hypothetical and invisible rewards

The main effect of brain activation to hypothetical rewards is identified from experiment 1 by contrasting stimuli predicting reward with stimuli predicting no reward. The reward in this comparison consisted of visually presented or imagined hypothetical monetary reward (20 pounds money bill) together with an invisible real pay-off (5 pence). We found a main effect for reward-related activation in the medial orbitofrontal cortex (OFC) and the midbrain (Figure 3, Table 1). Activation in the ventral striatum did not survive small volume correction but was present at a lower threshold (Figure 3, Table 1). When

tested individually, reward-related activation was observed in the medial OFC and the midbrain in visual presentation and imagination trials, respectively (Figure 4, Table 1). However, direct comparison of visual presentation and imagination trials did not reveal differential activations in any of the ROIs even at the exploratory threshold ($p<0.005$, $k=10$ voxels). At this exploratory threshold, we found overlapping, common activation in the midbrain ($p = 0.07$, small volume corrected) in the imagination and visual presentation trials using conjunction analysis (Nichols et al., 2005). These results indicate that hypothetical monetary rewards (irrespective of whether they are visually presented or imagined) enter associations with predictive stimuli and thereby activate reward regions even though the real pay-off is small.

Graded activation to hypothetical rewards.

The second experiment investigated the effect of parametrically increasing the value of the visually presented hypothetical reward (10 pence, 1 pound, 10 pounds) without increasing the real pay-off (5 pence). Two modes of hypothetical rewards were used - pictures of real money or alphanumeric displays of the corresponding value. By displaying the real cumulative take-home amount of money, we ensured that the brain responses reflect the effect of increasing the hypothetical monetary rewards. A linear contrast compared the stimuli predicting 10 pounds to stimuli predicting 10 pence. The contrast weight for reward display of 1 pound was set to zero, thus served as a middle point. Graded activation in the midbrain was observed with this contrast irrespective of whether the hypothetical rewards were alphanumeric or pictorial (Figure 5, Table 1). We did not find activations in other ROIs even at the exploratory threshold. The opposite contrast comparing 10 pence > 10 pounds with 1 pound as middle point did not yield any activations in our ROIs even at an exploratory threshold. We also tested an ROI in the striatum that included the dorsal striatum and did not find any activation for the contrast of interest. These results indicate that the midbrain activation reflects increasing magnitude of hypothetical monetary rewards although the real pay-off is kept constant.

Discussion

This research investigated brain activations to hypothetical monetary rewards that displayed an increased value of monetary rewards without in fact increasing the actual reward paid to the subject. The results show activations in the medial orbitofrontal cortex and the midbrain in processing visually presented and imagined hypothetical monetary rewards. Further, midbrain activation increased in a graded fashion with increasing amounts of hypothetical monetary rewards. Our results suggest that the use of hypothetical monetary rewards could be adopted as a generic technique for performing neuroimaging studies on reward.

Monetary rewards in neuroimaging studies

Functional neuroimaging studies using monetary rewards have found the same brain regions as those involved in processing primary rewards (e.g. Valentin & O'Doherty, 2009; Tobler et al., 2007; Kim et al., 2011). These and other previous studies have used varied experimental procedures to determine the way subjects receive monetary rewards. For instance, a consolidated amount is paid for participation and the reward is not contingent on the subject's performance (e.g. Boettiger et al., 2007; Schonberg et al., 2010). Another approach would be to use both monetary gains and losses (e.g. Delgado et al., 2005; Kim et al., 2006) so that the total money payable to subjects at the end of the experiment is not very large. Subjects might prefer (infrequent) large rewards compared to cumulative (frequent) small rewards. Hence, some paradigms use probabilistic rewards or randomly pick one of the decisions made about large rewards by the subject (e.g. Hsu et al., 2005; Pine et al., 2009).

Hypothetical monetary rewards (see also Bickel et al., 2009; Dreher et al., 2006; Kuhnen & Knutson, 2005) offer a good alternative to these methods of payment to subjects, as it offers stringent control to experimenters without having to resort to deceiving subjects, using probabilistic outcomes or losses, or treating trials differently. An unavoidable limitation of the approach used in our experiments is that the magnitude of the displayed

reward covaried with the hypothetical monetary reward. To account for this, participants were explicitly informed about the actual reward they would receive in each trial. Using hypothetical rewards also overcomes the issue that the real value of monetary rewards given every trial (e.g. 5p) has to be very small. It brings together psychological theories that postulate a positive reinforcement such as an OK signal is sufficient to drive behaviour, and economic theories that suggest monetary reward is crucial to positively drive behaviour (Camerer & Hogarth, 1999), as long as the monetary reward is not too small (Gneezy & Rustichini, 2000). As an extension of our approach, it would be interesting to compare the receipt of positive reinforcement signals and other forms of hypothetical rewards such as receiving 'points'.

Reward regions activated by hypothetical monetary rewards

Experiment 2 revealed graded activations in the midbrain to stimuli predicting different reward denominations (Figure 5, Table 1). The design of this study allowed us to dissociate the visual aspects of the monetary rewards from the value attached to them by using both alphanumeric and pictorial representations. The activation observed in the midbrain occurred in a region that also responds to primary liquid and food reward (Schultz, 1998). Similar activations occur in midbrain neurons of humans with monetary rewards (Zaghloul et al., 2009).

The graded activations in midbrain to increasing hypothetical rewards occurred despite the fact that each trial resulted in the same real pay-out. One possibility to account for this finding is that the reinforcing properties of money are so strong that when tested under extinction (such as delivering 5 pence when displaying 5 pounds, thus artificially decreasing the value of displayed reward), the responses do not extinguish. In other words, the graded responses comply with the displayed reward magnitude, instead of diminished responses to the extinction procedure. Such resistance to extinction would be reminiscent of the effects of drugs of abuse on instrumental behaviour (e.g. Quick & Shahan, 2009).

Experiment 1 revealed activation in medial OFC to visually presented hypothetical monetary rewards (Figure 4, Table 1). Previous neuroimaging studies have found a role for OFC in outcome valuation (Elliott et al., 2008; Chib et al., 2009; Peters & Büchel, 2009, 2010; Sescousse et al., 2010) and a medio-lateral distinction in processing rewarding and aversive stimuli (Elliott et al., 2000; O'Doherty et al., 2001; Kringelbach & Rolls, 2004). The activation in the medial OFC to stimuli predicting visually presented rewards is consistent with these earlier findings. However, at the employed statistical thresholds we did not find activations in the medial OFC ROI to increasing hypothetical reward. The outcomes in terms of real pay-off were the same irrespective of the displayed reward. Hence, it could be the case that the medial OFC is not differentially engaged when the actual outcomes do not differ.

In our two experiments, we did not observe reliable activations in the ventral striatum at the employed thresholds. Experiment 1 revealed a main effect for reward in the ventral striatum at an exploratory threshold (Figure 3, Table 1). At this threshold, activation in ventral striatum was observed in visual presentation trials (Table 1). In experiment 2, we did not find increasing activation in ventral striatum with increasing hypothetical rewards. Earlier neuroimaging studies have implicated the ventral striatum in representing reward value (Knutson et al., 2001; Peters & Büchel, 2009, 2010) and in reward prediction error (Pagnoni et al., 2002; McClure et al., 2003; Tobler et al., 2006; Hare et al., 2008). In a temporal discounting paradigm with similar hypothetical monetary rewards as in our experiments, ventral striatum activation showed differential discounting depending on the magnitude of the reward (Gregorios-Pippas et al., 2010). The real pay-offs in Gregorios-Pippas et al. (2010) were proportional to the displayed reward, whereas in our experiment, the real pay-off was constant irrespective of the displayed reward. Hence, it could be the case that, similar to medial OFC, the ventral striatum is not differentially engaged when the actual outcomes do not differ.

Together, the absence of graded responses in medial OFC and ventral striatum (see Peters & Büchel, 2010) suggests that hypothetical rewards could be less efficient in eliciting

increasing activations with increasing reward magnitude. A direct comparison of neural responses between increasing monetary reward and increasing hypothetical reward would be an interesting extension of our study.

Imagination of hypothetical monetary rewards

A novel contribution from our study is the investigation of experienced and imagined rewards. We found activation in medial OFC and midbrain to stimuli predicting visually presented and imagined rewards, respectively, though these activations were not significantly different among the two conditions (Figure 4, Table 1). Bray et al. (2010) found activation in medial OFC when participants imagined items they found personally rewarding. In the present study, we found reliable midbrain activation extending bilaterally in the imagination trials. Our findings suggest a possibility of common neural activation in the midbrain for imagined and (albeit slightly less strong in) visually presented rewards. It is of interest that no other activation was found to be common outside this ROI in a whole brain exploratory analysis. One reason for the discrepancy between our findings and those of Bray et al. (2010) could be due to the short duration of reward in the current study that limited the generation of vivid mental images as opposed to the longer duration used in the block design of Bray et al. (2010).

A key limitation of our study is that we cannot dissociate common activation, if any, between visually presented and imagined trials to be due to the imagination of hypothetical reward or the common receipt of invisible reward (i.e. 5 pence). Our findings also have to be interpreted in view of the limited power provided by the relatively small number of participants (n=12). Including more participants should be a consideration for future studies according to current practices in neuroimaging. Further, the image acquisition was done at a lower spatial resolution of 3.75 x 3.75 x 5 mm^3. Higher resolution of functional imaging would be desirable when focusing of regions such as the midbrain (D'Ardenne et al., 2008).

While our data are somewhat suggestive about common neural activations for reward-related visual imagery and perception, Kosslyn et al. (1996) did not find common brain areas affected by aversive stimuli during imagery and perception in their positron emission tomography (PET) study. Bray et al. (2010) have demonstrated a role for medial OFC in reward imagination. Contrary to those studies, we have used an event-related design with randomized trials of reward imagery and perception. The difference between these diverse findings regarding common neural activity may point to subtle differences in the imagination of outcomes of different valence, although the differences could also be due to methodological differences, such as the higher temporal resolution of fMRI compared to PET. Further studies using both rewarding and aversive stimuli with the same methods in the same participants would be required to corroborate this potential difference.

Theories of mental imagery disagree on whether the content of mental images and percepts are visual depictions (Kosslyn, 1988) or abstract propositions (Pylyshyn, 2002). We verbally instructed participants at the outset that all stimuli associated with reward presentation and imagination would result in the same amount of reward at the end of the experiment. Hence, participants may have imagined verbal rather than visual contents. To more fully address the mental contents of reward imagination, future research may want to dissociate propositional and visual reward imagination more explicitly. As a further extension, it would also be interesting to compare imagination of abstract reinforcers such as money to more primary rewards such as food reward or erotic stimuli (e.g. Simmons et al., 2005; Sescousse et al., 2010).

In summary, we propose that despite their limitations, monetary rewards can be used to study the human reward system in a straightforward manner. This technique is particularly useful to show participants monetary rewards with some buying power so that reward responses are maintained and avoid disappointment or frustration induced by the small value of money otherwise given at single trial levels.

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Figure Legends

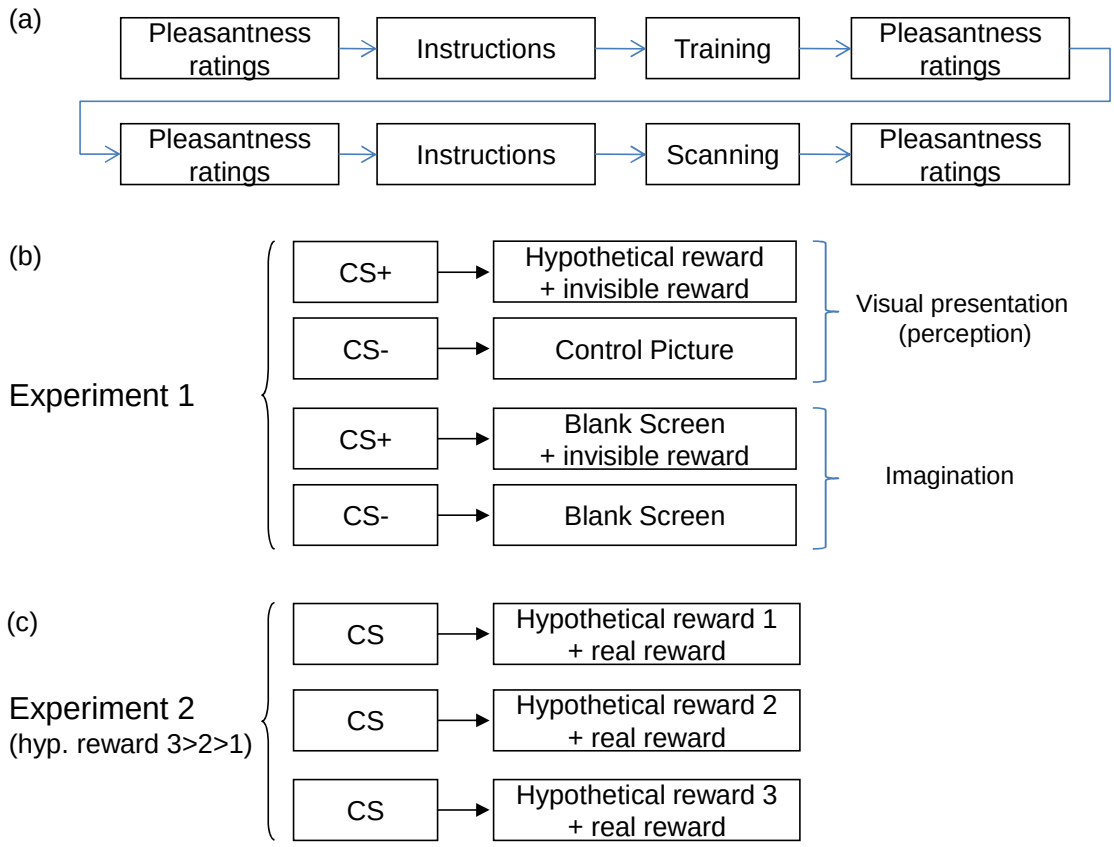

Figure 1: Experimental design and behavioural results.

(a) Training and Scanning schedule. Participants were trained up to one week before the scanning session using exactly the same stimulus-reward contingencies. In the first experiment, the instructions to imagine were given in a customized instruction sheet showing the stimulus – reward contingencies for every participant. They reported after every trial what they had seen or imagined using a button press. Participants performed an additional testing task immediately after the training of the second experiment. The training and scanning sessions for the two experiments were identical except that the training sessions had only half the number of trials. Pleasantness ratings for abstract stimuli were collected at the beginning and end of training and scanning sessions. The training and scanning sessions took place on different days separated up to one week. The

first experiment was always at the end of the session for those participants who took part in both experiments.

(b) Experiment 1. Four conditional stimuli were associated with either rewarding or non-rewarding pictures visually presented on the screen or to be imagined during a blank screen. Participants were instructed before the start of the experiment to imagine the corresponding reward or non-rewarding picture when the blank screen appeared. To ensure minimal demand effects, an invisible actual reward was given for every rewarding trial. The invisible reward was by two orders of magnitude smaller than the hypothetical reward picture and participants were fully informed of this manipulation at the start of the experiment. The contents of visual presentation and imagination were recorded by self-report on every trial.

(c) Experiment 2. Three conditional stimuli were associated with three hypothetical rewards that yielded the same actual reward. Two modes of reward presentation were used for hypothetical rewards – alphanumeric and pictorial. The actual reward was not displayed to the participants but added to the total take-home sum that was continuously displayed at the bottom of the screen throughout the experiment.

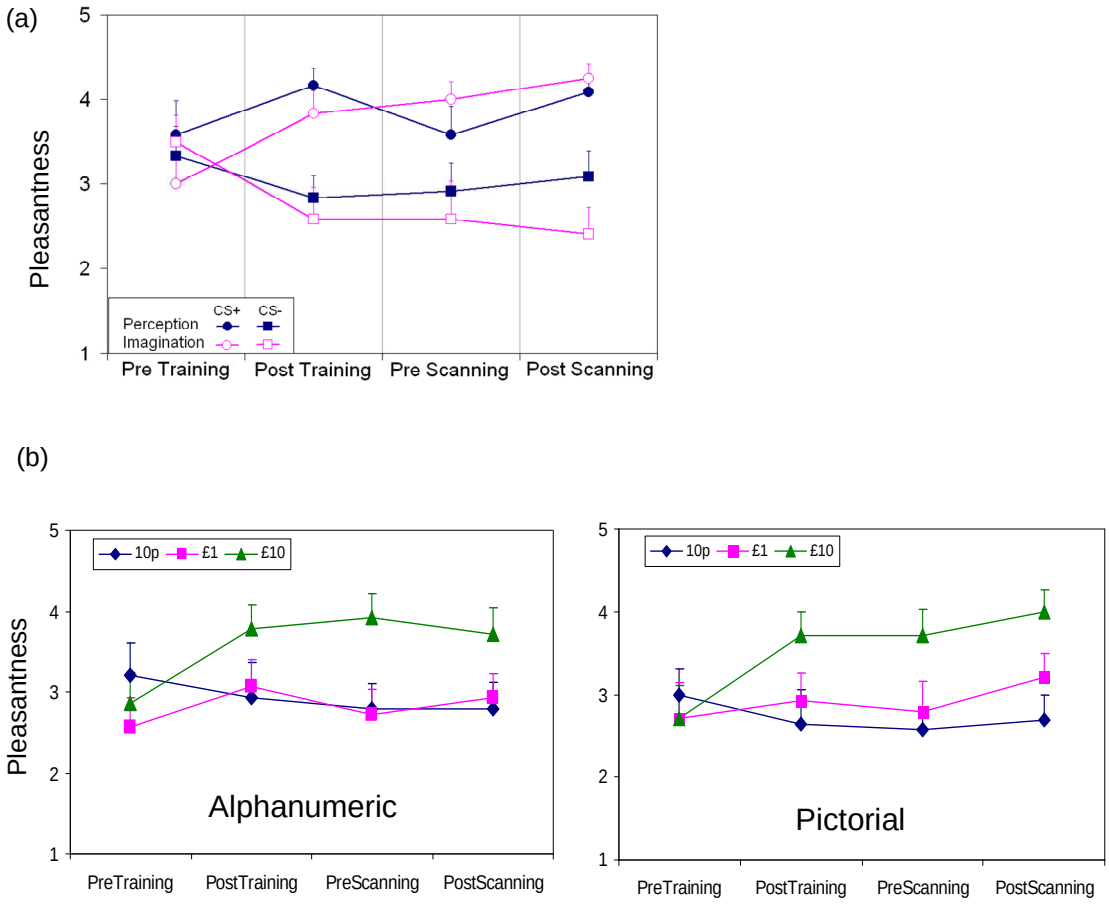

Figure 2: Pleasantness ratings. (a) Pleasantness ratings for four conditional stimuli in experiment 1 on a scale of 1 (dislike very much) to 5 (like very much). Pretraining took place up to one week before the scanning session. (b) Pleasantness ratings for the six conditional stimuli predicting three hypothetical rewards in alphanumeric (left panel) and pictorial (right panel) modes of presentation.

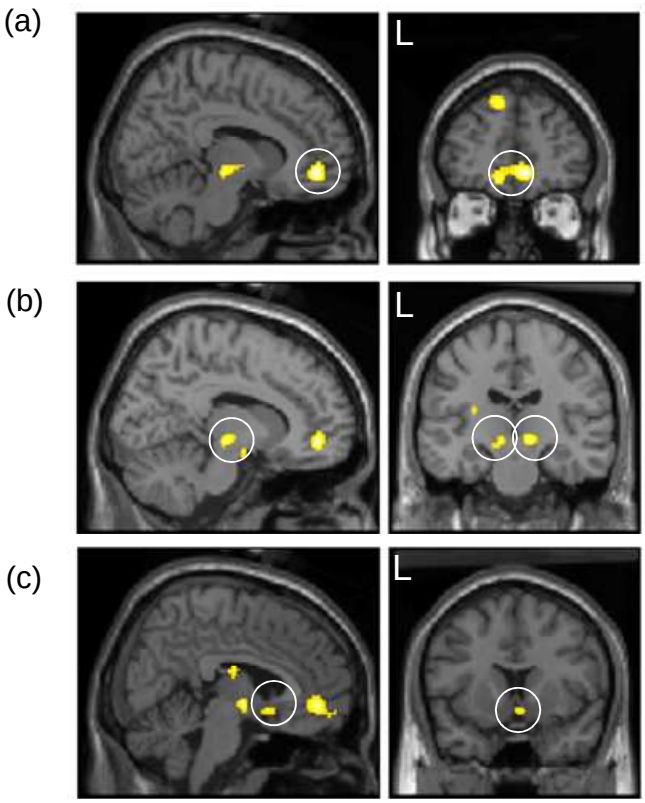

Figure 3: Main effect of reward – related activation. Activation in (a) medial orbitofrontal cortex (b) midbrain and (c) ventral striatum for reward compared to no reward in experiment 1. The activation maps are thresholded at $p<0.005$ and an extent threshold of 10 voxels for display purposes. Note that activations are displayed for the whole brain and the anatomical ROI masks are not used in the figures.

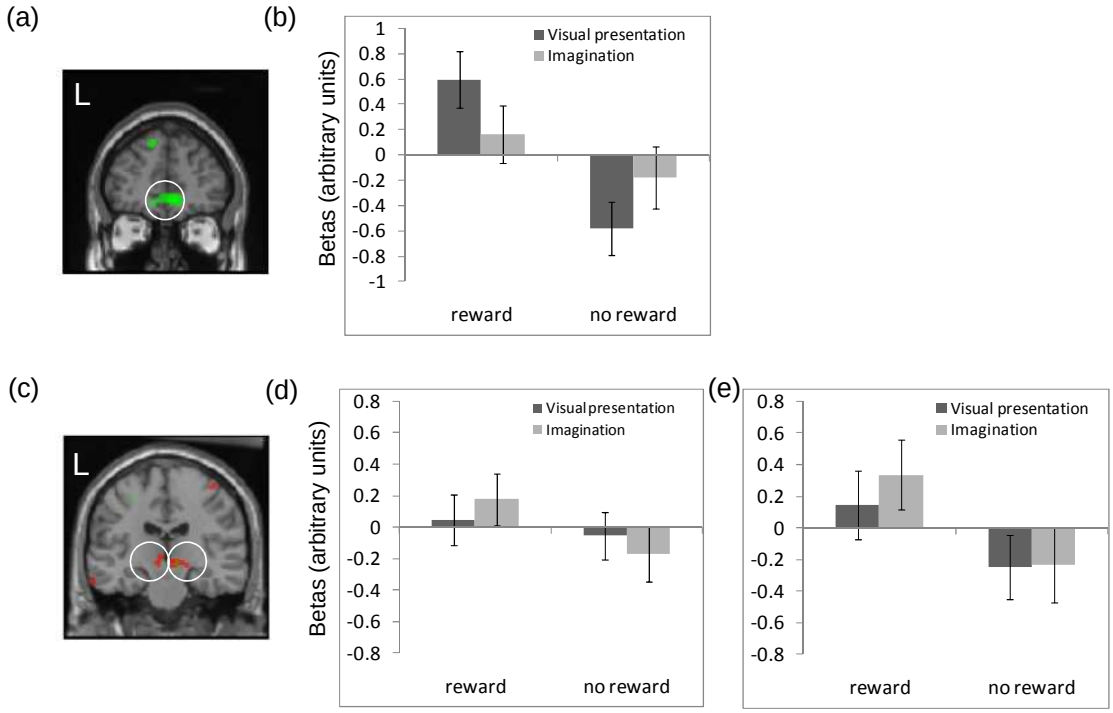

Figure 4: Activation to visually presented and imagined rewards. (a, b) medial orbitofrontal cortex (OFC), (c-e) midbrain. Activation is shown in green for visual presentation condition and in red for imagination condition. See the legend of Figure 3 for thresholding information. The corresponding contrasts of parameter estimates (betas) are plotted in (b) medial OFC, (d), left and (e) right midbrain.

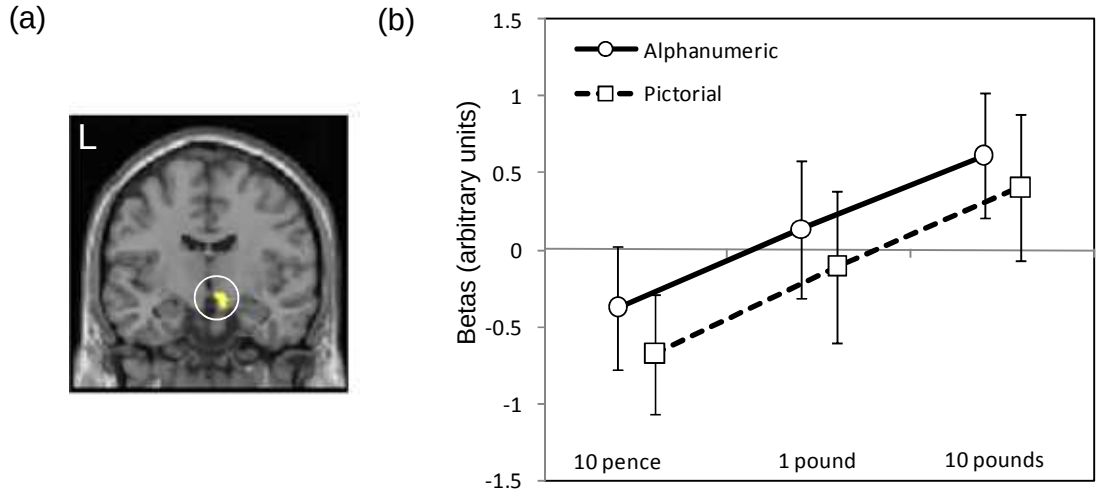

Figure 5: Graded activation in the midbrain to hypothetical rewards in experiment 2 and the corresponding plot of parameter estimates (betas). See also the legend of Figure 3 for thresholding information.

Table 1: Location of peak activations in regions of interest (ROIs). Extent of activation (cluster size) is reported at uncorrected threshold of p<0.005 and the number of voxels surviving small volume correction for height of activation is also given.

Contrast	ROI	MNI coordinates (mm)			Z score	Cluster size	
		x	Y	Z		uncorrected	ROI corrected
Experiment 1							
Main effect: reward > no reward							
	Medial OFC	10	46	-8	4.14	254	32
	Midbrain	12	-18	-6	3.46	56	3
		-6	-8	-12	3.13	68	0
		-8	-18	-6	3.12		
	Ventral Striatum	6	10	-10	2.85	37	0
Visual presentation (reward > no reward)							
	Medial OFC	10	46	-8	4.17	246	35
	Midbrain	10	-20	-6	3.10	12	0
	Ventral Striatum	2	12	-12	3.44	80	0
Imagination (reward > no reward)							
	Midbrain	-6	-10	-6	3.54	80	8
		8	-20	-6	3.46	43	1
Conjunction: Visual presentation AND Imagination (reward > no reward)							
	Midbrain	10	-20	-6	3.10	11	0
Experiment 2							
Main effect: 10 pounds > 10 pence							
	Midbrain	10	-10	-12	3.52	55	4
Alphanumeric (10 pounds > 10 pence)							
	Midbrain	4	-16	-8	2.92	22	0
		-4	-16	-10	2.81	19	0
Pictorial (10 pounds > 10 pence)							
	Midbrain	8	-26	-12	2.80	4	0